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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/673,555	02/13/2001	Jacques Benveniste	9320.113USWO	8541

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EXAMINER
CHUNDURU, SURYAPRABHA

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 09/11/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/673,555	BENVENISTE ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-72* is/are pending in the application.

4a) Of the above claim(s) *24-27,36-41 and 65-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23,28-35,42-64 and 69-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
4)☐ Interview Summary (PTO-413) Paper No(s) _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other

DETAILED ACTION

1. Applicants' response to the office action and amendment (Paper No. 15) filed on June 21, 2002 has been entered.

Response to Arguments

2. Applicant's response to the office action (Paper No.15) is fully considered and deemed persuasive in part.

3. The objection to the specification made in the previous office action is withdrawn in view of the amendment (Paper No. 15).

4. The following rejection made under 35 U.S.C. 112 second paragraph in the previous office action are maintained herein:

(i) Claims 1-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims recite a phrase "electromagnetic signal characteristic of the biological activity" which is confusing and unclear as what the phrase refers to because any light or florescence spectrum releases electromagnetic signal and it is not clear how a signal be characteristic of biological activity, an absorbance reading of a biological or a chemical reaction by spectrophotometer could be an electromagnetic signal. The definition for this phrase in the specification is indefinite and reads on any photochemical reaction. Therefore, the metes and bounds of the claims are unclear.

Response to Arguments:

Applicants' arguments to the above rejection are fully considered and are found not persuasive because (i) it is unclear how a signal be characteristic of biological activity since a

signal intensity is measured as proportional to the biological activity in any biochemical reactions. It is not clear whether the electromagnetic signal as recited in the specification does or does not correlate with the biological activity. Further it is not clear how the EM signal is considered to characterize the biological activity. Therefore, the rejections are maintained herein.

5. With respect to the rejection made in the previous office action under 35 U.S.C. 102(b), Applicant's arguments and amendments have been considered but are found not persuasive.

The following is the rejection made in the previous office action under 102 (a), 102(b) and 102(e):

a. Claims 1-23, 28-31 are rejected under 35 U.S.C. 102(a) as being anticipated by Benveniste et al. (FASEB J., March 17, vol. 12(4); pp A412, 1998).

Benveniste et al. teach a method to detect electromagnetic signal of biological systems wherein Benveniste et al. disclose that the method comprises bringing into contact ligand (agonist) with receptor (target cell), applying electromagnetic signals and detecting the electromagnetic emittion of specific hertzian waves emitted by these pair of molecules and detecting the signal(s) by digitally recording on a multimedia computer, as an indication of biological activity (see A412, column 1, abstract 2392). Further Benveniste disclose that this method can be applied to biology and medicine (see abstract 2392). Thus the disclosure of Benveniste et al. meets the limitations in the instant claims.

b. Claims 1-23, 28-35 and 42-64, 69-72 are rejected under 35 U.S.C. 102(b) as being anticipated by Benveniste et al. (J Allergy Clin Immunol., vol. 99 (1), part 2, pp S175, 1997).

Benveniste et al. teach a method of digitally amplifying electromagnetic signal of biological molecules wherein Benveniste et al. disclose that the method comprises bringing into

contact ligand (agonist) with receptor (target cell), applying electromagnetic signals in a solvent (water) to detect molecular activity (see page S175, column 1, abstract 705). Further, Benveniste et al. disclose recording digital 22kHZ (kilo hertzs) by a transducer and computer with soundcard (see page S175, column 1, abstract 705); the method can be applied to chemistry, biology and medicine. Thus the disclosure of Benveniste et al. meets the limitations in the instant claims.

c. Claims 1-23, are rejected under 35 U.S.C. 102(b) as being anticipated by Hollis et al. (USPN. 5,653,939).

Hollis et al. teach a method for identifying molecular structures (includes ligand-receptor, antigen-antibody, DNA-probe) wherein Hollis et al. teaches contacting a probe with target site facilitating binding of probe to the target to form a binding complex, applying electrical or optical signals to the test sites, and detecting signals associated with the molecular structures (see column 1, lines 18-25, column 2, lines 30-38 and 59-67). Further, Hollis et al. discloses that (i) the method includes electromagnetic wave detector to detect the test sites bonded target-probe pairs based on resonant frequencies (see column 8, lines 32-57); (ii) the method can be used in detecting antigen-antibody binding (see column 18, lines 3-26 and table III). Thus, the disclosure of Hollis et al. meets the limitations in the instant claims.

d. Claims 1-23, are rejected under 35 U.S.C. 102(e) as being anticipated by Gold et al. (USPN. 6,242,246).

Gold et al. teach a method for the detection of a target molecule binding to nucleic acid ligand using fluorescence methods wherein Gold et al. disclose that the method comprises contacting protein target molecules with labeled nucleic acid ligands on the surface of a biochip and detecting the signal generated by the said target –ligand binding through a signal-amplifying

hybridization cascade (see column 10, lines 33-67, column 11, lines 1-21, and column 14, lines 26-57). Further Gold et al. disclose the detection of the signal could be carried out using surface plasma resonance wherein resonance is measured using biosensors (see column 18, lines 9-41). Thus the disclosure of Gold et al. meets the limitations in the instant claims.

Response to Arguments:

Applicant's arguments with respect to the rejection made under 35 U.S.C. 102 (a), 102(b) and 102(e) have been considered and are found not persuasive. Applicants argue that the method claimed is distinct from the method in the prior art. This argument is unavailing for two reasons. First, the prior art references teach each of the limitations found in the claims. Second, the claim is of the open "comprising" format, which permits the inclusion of additional elements, so that any additional steps are permitted in the claim.

Applicants particular argument that the prior art Benveniste et al. (FASEB J., vol.12 (4): ppA412, 1998) (I) and Benveniste et al. (J Allergy Clin Immunol., vol. 99(1), part 2, pp S175, 1997) (II) did not teach amplification of the reaction, is found not persuasive because the instant claim recites applying electromagnetic (EM) signal ' prior to, simultaneously with, or subsequent to said ligand and said receptor being brought into contact. The instant claims read on applying EM subsequent to the formation of ligand-receptor complex. Hence the prior art meets the limitation 'subsequent to the reaction'. Further, the prior art I teach activation of biological systems using electromagnetic signal, which implies that EM activates or increases or amplifies reaction between two biological molecules. Prior art II teaches that water transmits electronic signals to molecules amplification of these molecular signals digitally and recording the signals

through computer networking. Thus both prior arts of record support the amplification of reaction through EM. Hence the rejection is maintained herein.

The prior art of the record Hollis et al. (USPN. 5,653,939) and Gold et al. (USPN. 6,242,246) also support the limitation ' applying EM subsequent to the formation of ligand-receptor complex which facilitates in increasing the binding of the complex. Thus the rejections are maintained herein.

New Grounds of Rejections

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-23, 28-35, 42-64, 69-72 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CA FC 1988). Wands states at page 1404,

" factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the

presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims".

The nature of the invention

The claims are drawn to a method of amplifying a reaction between a ligand and a receptor of a ligand-receptor pair comprising applying electromagnetic (EM) signal characteristic of biological activity to at least one of the said pair and amplifying or increasing the reaction process of formation of the said ligand-receptor complex. The invention is a class of invention, which the CAFC has characterized as "the unpredictable arts such as chemistry and biology." Mycogen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Fed.Cir.2001).

The breath of the claims

The claims encompass a method of increasing the formation of a ligand-receptor complex by applying electromagnetic (EM) signals characteristic of biological activity to said pair or at least to one member of the pair. No specific type of electromagnetic signal characteristic of biological activity is recited in the specification and thus the claims encompass all electromagnetic signal generating sources such as UV, infra-red, x-rays and visible wave length rays to apply to the said pair. No specific EM signal is recited that is characteristic of biological activity. EM signals picked up by the ligand-receptor complex does not reasonably provide enablement for biological activity associated with ligand-receptor complex formation when EM is applied. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Quantitation of Experimentation

The quantitation of experimentation in this area is extremely large since amplification of EM signals characteristic of biological activity would require, initially, in vitro to demonstrate proof of the principle. That is prior to any result intervention, it would be necessary to create a biological molecule which is active as recited in the specification which could be activated or show increase in activity or the effect of EM signal on the active biological molecule, then show this effect would have some potential effect of in a reaction process with these active biological molecules, a series of showings not present in the specification. Following such experimentation, analysis involving clinical samples would need to be characterized, an inventive, unpredictable and difficult undertaking in itself, and efficacy would need to be demonstrated in such analysis. This would require years of inventive effort, with each of the many intervning steps, upon effective reduction of practice, not providing any guarantee of success in the succeeding steps.

The unpredictability of the art and the state of the prior art

The art teaches that the field of biology related to EM is, one of the most unpredictable areas of human endeavor for which patents are sought. Galvanovskis et al. (Biophys J., vol. 73(6) pp. 3056-3065, 1997) writes that "cells may respond to the exposure of low-frequency electromagnetic fields with changes in cell division, chemical reaction rates etc. The chain of events leading to such responses is difficult to study, mainly because of extremely small energies associated with low-frequency fields, usually much smaller then the thermal noise level". Galvanovski et al. explored this possibility for ion channel model and showed that to detect even very weak low-frequency electromagnetic signals (<100 Hz and down to 100 microT) in cellular system it requires a large number of ion channels.

The prior also supports the unpredictable nature of the art associated with biological molecules. Thus prior art not only fails to support the efficacy of the invention, but in fact, supports the unpredictability.

Working examples

The specification has no working examples to show application of EM amplifies biological activity of ligand-receptor complex.

Guidance in the Specification

The specification solely teaches the increase in the indexes of complex formation when the EM signal is applied, and provides absolutely no teaching or suggestion regarding any characterization of biological activity based on EM signals picked up the complex, nor are any amplification of EM signals in the said reaction which are picked up by unreacted biological molecules (ligand alone or receptor alone) of the pair or other biological molecules of the reaction. No specific teachings regarding the use of any ligand-receptor pair in characterizing biological activity except the identification of E.coli antigen-antibody complex formation.

Level of Skill in the art

The skill in the art is deemed to be high.

Conclusion

In the instant case, as discussed above, the level of unpredictability in the art is high (see Galvanovskis et al., Biophys J., vol. 73(6) pp. 3056-3065, 1997) , the specification provides one with no guidance that leads one to a reliable method to characterize biological activity. One of the skill in the art cannot readily anticipate the effect of a change within the subject matter to which the claimed invention pertains. Further the specification does not provide guidance to

overcome art recognized problems in this field of biology. Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of any working examples and the negative teachings in the prior art balanced only against the high skill in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to perform the method of the claim as broadly written. Until some actual and specific significance can be attributed to define biological characteristic based on EM signal in the specification, one of ordinary skill in the art would be required to perform additional experimentation to make and use the invention as broadly claimed. It would require extensive experimentation involving testing to determine whether any particular region of the elements of the pair would be functioned as required by the claims to characterize biological activity.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
September 5, 2002

JEFFREY FREDMAN
PRIMARY EXAMINER